

BRIEF COMMUNICATION

Klippel-Feil syndrome with other associated anomalies in a medieval Portuguese skeleton (13th–15th century)

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Abstract

Klippel-Feil syndrome, or synostosis of the cervical spine, is the result of an abnormal division of somites during embryonic development. This report analyses an adult male (exhumed from a Portuguese graveyard dating from the 13th to the 15th century) with malformations in the cranium and vertebral column. Besides the lesions that are typical of Klippel-Feil syndrome type II, other defects usually linked to this pathology are described (occipito-atlantal fusion, hemivertebrae, butterfly vertebrae, cervical rib, changes in normal number of vertebral segments and a possible Sprengel deformity).

Key words butterfly vertebra; hemivertebrae; Klippel-Feil syndrome; medieval Portuguese skeleton.

Introduction

During embryonic development, subdivision of the paraxial mesoderm into hemimetameric block-like masses (the somites) occurs by day 20. This formation continues cephalocaudally until day 30 of embryo growth (Clarke et al. 1998; Scheuer & Black, 2000). By this time, some structural developmental field defects may arise from a variety of genetic and epigenetic factors (Barnes, 1994). One of these defects corresponds to an abnormal division of mesodermal somites, namely an inhibition or necrosis of the chondrogenic centres of the vertebrae (González-Darder et al. 2002). This results in a congenital fusion of two or more cervical vertebrae, Klippel-Feil syndrome (KFS), also known as synostosis of cervical spine (Martin, 1994; Clarke et al. 1998; Jones & Mayer, 2000; Larson et al. 2001). This disease was first described in 1912 by Maurice Klippel and Andre Feil in a clinical case with massive cervical vertebrae fusion. In 1919 Feil proposed three different types of KFS based on the location and amount of fusion (Barnes, 1994; Larson et al. 2001). Later, Clarke and co-authors (1998) suggested another classification, where the defects are distinguished by inheritance mechanisms (Clarke et al. 1998).

The classic clinical triad of KFS is a short neck, a low posterior hairline and limitation of neck movements, especially lateral ones (Larson et al. 2001; González-Darder

et al. 2002; Thompson & Scoles, 2002). Occasionally, the trapezius muscles are very prominent, conferring a winged aspect to the neck (Fishman, 1979; Turek, 1991; Jones & Mayer, 2000). Congenital fusion of cervical vertebrae is sporadic, but seldom may be inherited (Clarke et al. 1998; Larson et al. 2001). Most studies indicate that KFS is an uncommon disorder; some authors indicate that this kind of defect is present in 0.5% (Clarke et al. 1998) or 1% (Jones & Mayer, 2000) of births, but others suggest a much lower rate of approximately 1:40 000 (González-Reimers et al. 2001; Larson et al. 2001).

Other anomalies may, separately or together, be associated with KFS. The most common are Sprengel deformity, scoliosis or kyphosis, spina bifida, cleft palate, hemivertebrae (Aufderheide & Rodríguez-Martín, 1998), deafness or hearing impairment (Jones & Mayer, 2000), genitourinary defects (Thompson & Scoles, 2002), malformation of the atlas and axis, platybasia and basilar impression (Fishman, 1979). Some rarer diseases have also been reported with KFS, some being very serious with severe clinical consequences to the patients (Holmes, 1990; Turek, 1991; Martin, 1994; Aufderheide & Rodríguez-Martín, 1998; Clarke et al. 1998; Jones & Mayer, 2000; Thompson & Scoles, 2002; Pany & Teschler-Nicola, 2006).

Materials and methods

The lesions presented in this study were observed in a skeleton, designated RMPE-73, recovered from a medieval graveyard in Estremoz, SE Portugal. Radiocarbon dating, using two other individuals, pointed to a time period between the 13th and the 15th century (for 2 Sigma, with 95% probability). This archaeological series was not identified, i.e. there were no records, therefore age and

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Fig. 1 Left hemivertebra (C0) fused to the occipital condyle and with the foramen magnum. The arrow shows an articular area resulting from contact with the odontoid process (inferior view, scale of 1 cm).

sex were determined applying the usual macroscopic methods from biological and forensic anthropology (Ferembach et al. 1980; Lovejoy et al. 1985; Brooks & Suchey, 1990; Bruzek, 2002).

Exhaustive macroscopic observations were performed on the skeleton in order to describe the lesions as well as to identify other anomalies. The diagnostic was confirmed by computed tomography.

Results

This individual corresponds to a male with a biological age between 30 and 45 years. The cranium and cervical column show several severe abnormalities: in the number of vertebral elements (8 cervical, 11 thoracic, 6 lumbar and 5 sacral) and in their segmentation and morphology.

The first cervical element, a left hemivertebra (C0), is fused to the occipital condyle as well as with the foramen magnum (Fig. 1). Apart from a small cleft in the anterior portion, the union is complete. Medially to the left articular facet, another articular area is observed resulting from the contact with the odontoid process.

C1 is not merged at the sagittal plane, neither in the anterior face nor in the posterior one. The result is an atlas composed of two unfused hemivertebrae. On the other

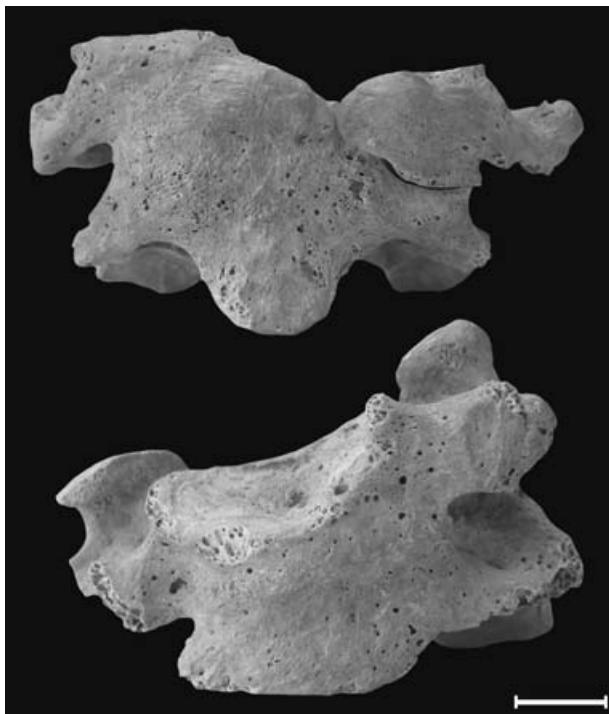


Fig. 2 Two blocks of fused vertebrae: C1–C2 (upper) and C5–C6 (lower) (anterior view, scale of 1 cm).

hand, the right hemivertebra is merged with C2 (C1–C2 block), while the left free portion articulates normally with the adjacent elements (Fig. 2). The C1–C2 union affects the vertebral bodies and articular facets, developing a bone bridge between the arches. The axis also shows deformities in its hypoplastic odontoid process.

C5 and C6 are two wedge-shaped vertebrae that are incorporated in another vertebral block (Fig. 2) with union of bodies, right articular facets and right arches. Both vertebrae have their own left transverse process but share the right one. The CT scan shows a sagittal cleft in the central part of the body without neural arch involvement (Fig. 3). The intervertebral space only remains on the left side, although narrower than usual.

The transverse foramina are preserved but in some cases they are very narrow, especially in C6, which has a diameter of less than 1 mm.

Merged with the left transverse process of C7 there is a rudimentary cervical rib. C7 right side has post-mortem modifications, ruling out any observation of the same anomaly.

Concerning the thoracic region, abnormalities are present in the number of elements (11 instead of 12) and at T3 which has a cleft spinous process. All 11 thoracic ribs were found to be morphologically normal.

The lumbar segment was composed of six true vertebrae, without sacralization, since the sacrum has the normal five elements.

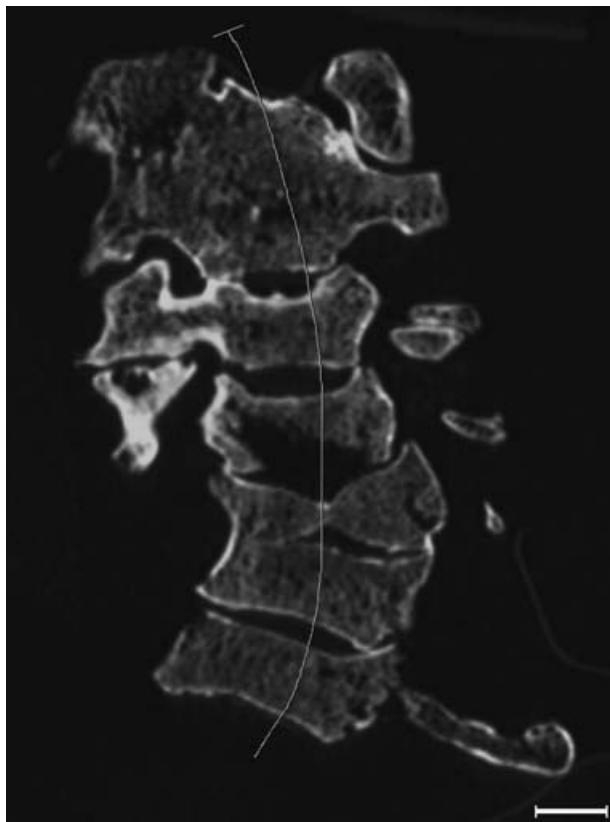


Fig. 3 CT scan showing the C1–C2 and C5–C6 vertebral blocks, C5 butterfly vertebra and cervical dextroscoliosis (scale of 1 cm).

Apart from the vertebrae, there are other asymmetries: (1) in the skull, with very slight differences in the outline of the nasal cavity; (2) in the upper limbs, where the difference between humeri length is approximately 15 mm; and (3) in the shoulder girdle. In this last case, some variations were noted in bone size and muscular attachment sites; however, the morphology of these bones is apparently normal. Asymmetries between the scapulae (elevation of the right shoulder) were observed during the excavation by the abnormal inhumation position (Fig. 4).

This skeleton shows two examples of scoliosis: a cervical dextroscoliosis (Fig. 5) and a thoracic levoscoliosis. In contrast to the appendicular skeleton, where degenerative diseases are absent or minimal, in the column these lesions are exuberant, both in osteoarthritis and enthesopathies. Macroscopically, there seems to be a difference in the



Fig. 5 Reconstruction of cervical column with dextroscoliosis (anterior view scale of 1 cm).

depth of the external acoustic meatus; nevertheless, the CT scan shows that there is no meaningful pathological difference.

Discussion

This congenital fusion of four vertebrae into two blocks (C1–C2, C5–C6) occurs when there is an abnormal division of somites, resulting in the disorder that we know as Klippel-Feil syndrome (Aufderheide & Rodríguez-Martín, 1998; Netter, 2002). According to Feil's classification, the case described here is consistent with type II KFS, where fusion of one or two interspaces is observed (Larson et al. 2001). The presence of hemivertebrae (C0, C1, C5 and C6) as well as occipito-atlantal fusion corroborates this diagnosis. Hemivertebrae occur when there is no proper development of the two ossification centres (Aufderheide & Rodríguez-Martín, 1998). In C0 (transitional vertebra at the occipito-cervical border), only one of two ossification centres

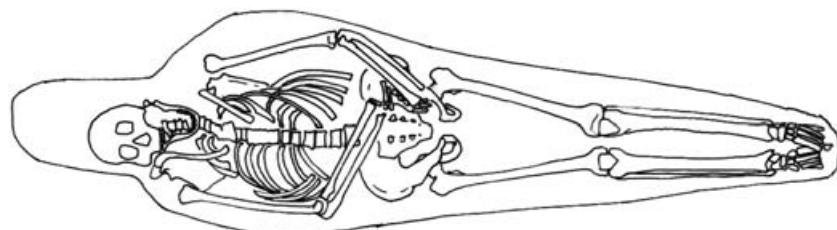


Fig. 4 *In situ* position of the RMPE-73 showing the elevation of the right shoulder.

developed, while in C1 the two centres did not fuse. In the first case, the asymmetry may disturb the weight-bearing equilibrium of the spine (Aufderheide & Rodríguez-Martín, 1998) leading to a dextroscoliosis and consequently to the observed osteoarthritis. The two blocks of merged vertebrae (C1–C2; C5–C6), the wedge-shaped vertebrae (C5–C6) and the sagittal cleft at the C5 vertebral body are also responsible for this lateral curvature and for the degenerative process in the cervical column.

Apart from the segmentation errors previously described (hemivertebrae and vertebral blocks), other paraxial mesodermal field defects coexist, specifically the cranial-caudal border shifting (Barnes, 1994). This alteration occurs in the transitional vertebrae, resulting in a cervical rib (cranial shift of the cervicothoracic border) and in numerical variation of the thoracic (11) and lumbar (6) elements (cranial shift of the thoracolumbar border).

The sagittal cleft in the centre of the C5 vertebral body is reported as a 'butterfly' vertebra that results because of a failure of the notochord to regress during the development of the vertebral segment. This is an uncommon defect, being more frequent in the thoracic and lumbar segments. Sagittal clefts may have some variability, from a narrow bifurcation (as in the present case) to a complete cleft (Barnes, 1994). It rarely has symptomatic significance (Aufderheide & Rodríguez-Martín, 1998), although it may be associated with defects in the gastrointestinal tract and nervous system, as well as other vertebral or rib defects (Barnes, 1994).

In a normal column the atlanto-occipital joint is responsible for flexion and extension, while the atlanto-axial joint allows rotation movements. These movements may have been compromised by the pathological modifications at the cranial base, atlas and axis.

The diameter reduction of the transverse foramina, the deformities in foramen magnum and cervical vertebrae may secondarily have led to a compression of the nervous roots as well as to other peripheral nervous system's symptoms, unless the vertebral artery could have passed outside (instead of inside) the foramina, which may occur when the transverse foramina are too narrow.

During the excavation, a marked elevation of the right shoulder was detected. Such elevation, when associated with asymmetries between scapulae, is interpreted as a failure of normal scapular descent known as Sprengel's deformity (Aufderheide & Rodríguez-Martín, 1998; Craig, 2000; Scheuer & Black, 2000; Netter, 2002; Thompson & Scoles, 2002).

The aetiology of Sprengel deformity is poorly understood (Aufderheide & Rodríguez-Martín, 1998; Scheuer & Black, 2000), but the underlying factors, whatever they are, act during the embryonic stage, after the formation of upper limb buds (Craig, 2000). The affected scapula is typically smaller and the distance from the acromion to the spine is shorter than in the normal side. Furthermore, the clavicle

is elevated laterally and may not develop its usual 'S' shape morphology, since it is the scapular descent that stimulates the clavicular bending (Craig, 2000). In some cases (25%), an omovertebral bone (*os omovertebrale*) connects the upper-internal portion of the scapula to the spinous process of a cervical vertebra (Aufderheide & Rodríguez-Martín, 1998; Craig, 2000). In the present study, morphological and morphometric asymmetries between scapulae were very slight and there was no omovertebral bone. Nevertheless the recorded shoulder elevation suggests a possible case of moderate Sprengel deformity, for three reasons: (1) there was no taphonomic evidence of burial disturbance; (2) the degree of scoliosis (which may lead to an abnormal posture) was too small to justify the high elevation angle of the right shoulder; and (3) Sprengel deformity occurs in 25 to 30% of patients with KFS.

The small asymmetries in the nasal cavity as well as in the humeri, excludes the possibility of pathological conditions such as Goldenhar syndrome.

Finally, it is necessary to remember that this is an archaeological specimen and consequently all observations were performed in dry bone. Therefore it is not possible to assess if there were other pathologies or complications only visible on clinical cases.

Conclusions

The set of cranium, vertebrae, ribs and shoulder girdle malformations seem to be a consequence of failures during the early embryonic development. This atypical morphology and segmentation of vertebrae is classified as KFS, an uncommon disorder resulting from an abnormal division of mesodermal somites. Of the defects known to be associated with this disorder, the case described here presents occipito-cervical fusion, hemivertebrae, butterfly vertebrae, cervical rib, changes in normal number of vertebral segments and a possible case of Sprengel deformity.

The instability caused by vertebral anomalies and scoliosis gave rise to severe degenerative lesions in the spine (osteoarthritis and enthesopathies) which do not affect the appendicular skeleton.

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